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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/235,875	01/22/1999	LARA MADISON	MBX020	2296

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EXAMINER

KALLIS, RUSSELL

ART UNIT

PAPER NUMBER

1638

DATE MAILED: 06/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/235,875

Applicant(s)

MADISON ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 17 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1,6,7,10 and 14-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,6,7,10 and 14-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

1. Claims 8-9, 11-13, 22-27 and 31 have been cancelled.
2. Claims 1, 6-7, 10, and 14-21 are pending.
3. The rejection of Claim 1 under 35 U.S.C. 102(b) as being anticipated by Peoples *et al.* U.S. Patent 5,534,432 published July 9, 1996 is withdrawn in view of Applicant's amendments.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### *Claim Objections*

5. Claims 14-21 are objected to because of the following informalities: Claims 14-21 are improperly depending from cancelled claims. Appropriate correction is required. Applicant has indicated by phone on 5/28/03 that Claims 14-18 are to depend from Claim 1 which also corrects the improper dependency for Claims 19-21.

#### *Claim Rejections - 35 USC § 112*

6. Claims 1, 6-7, 10 and 14-21 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official actions mailed 10/11/00, 3/26/01, 3/28/02 and 12/9/02. Applicants arguments filed 3/20/03 have been considered but are not deemed persuasive.

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Applicant asserts that they had possession of a method for the biological production of PHA containing 3-HH in *E. coli* comprising the transgenes of the invention and that the specific transgenes of the invention can be used to isolate other genes encoding the enzymes of the claimed invention (response pages 8-9); and structural features common to members of the claimed genus of pha genes have been determined by primer/oligo binding used to isolate such sequences (response page 9 and page 11); Gene isolation methods comprising hybridization or primer binding using a known gene does not define a genus of polynucleotides because the method does not provide the descriptive information for determining whether one is in possession of the invention because probe hybridization or primer binding to another DNA molecule does not entail a description of the isolated DNA molecule.

Applicant asserts that the broadly claimed categories of sequences of the claimed invention are available in public databases (response page 10). Applicant has not set forth a representative number of sequences that would define the invention. Applicant has sent along sequences with the current amendment taken from the NCBI database of which many were entered into that database after either the filing date or claimed priority date of the instant application some of which have only a putative function.

Applicant asserts that known substrates dictate the structural features within the pockets of each enzyme to which they bind (response page 11). Known substrates do not dictate the structural features of a binding pocket of an enzyme because there are many possible configurations of a binding pocket that will bind the substrate each to a varying degree utilizing different structural elements.

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7. Claims 1, 6-7, 10 and 14-21 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of production of a polyhydroxyalkanoate, polyhydroxybutyrate-polyhydroxyvalerate containing 3-hydroxyhexanoate, by growing a *E. coli* transformed with PHB polymerase from *A. caviae* and phbA thiolase and phbB reductase (phbAB) from *R. eutropha* genes (Example 5) or phbC polymerase from *R. eutropha* and phaJ D-specific enoyl-CoA hydratase from *A. caviae* genes (Example 4), does not reasonably provide enablement for a method of production of a polyhydroxyalkanoate, polyhydroxybutyrate-polyhydroxyvalerate containing 3-hydroxyhexanoate, by growing a bacterium with bacterial transgenes encoding an enzyme selected from the broadly recited groups of; any phbA thiolase gene encoding an enzyme that converts butyryl-CoA to acetyl-CoA, any phbB reductase gene encoding an enzyme that converts 3-ketohexanoyl CoA to beta-hydroxyhexanoyl-CoA, any phbC gene encoding an enzyme that polymerizes 3-hydroxybutyryl CoA, any D-specific enoyl-CoA hydratase, and any beta-hydroxy-ACP-coenzymeA transferase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official actions mailed 10/11/00, 3/26/01, 3/28/02 and 12/9/02. Applicants arguments filed 3/20/03 have been considered but are not deemed persuasive.

Applicant asserts that the enzymes do not interact physically with one another but rather substrates and enzymes do interact (response page 6); The Examiner acknowledges Applicant's assertion of biochemical theory, but would like to point out that there are examples in the literature of multienzyme complexes where there are protein-protein interactions (e.g. the

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dihydrolipoamide acetyltransferase and dihydrolipoamide dehydrogenase subunits of the *Escherichia coli* pyruvate dehydrogenase multienzyme complex) and of enzymes such as phosphatases interacting with kinases that are well known in the art.

Applicant asserts that the discovery that a broad range reductase and a polymerase that accepts more than one type of substrate could be used in a single pathway to synthesize PHB-co-HH was a completely unexpected and resulted in 1.0% HH co-monomer and that this pathway is predicated upon efficient substrate/enzyme interactions and reactions (response page 7). Since the polynucleotides encoding the claimed enzymes are to be isolated from a myriad of different sources, and since no other examples of unexpectedly successful combinations of "a broad substrate range reductase" and "a polymerase that accepts more than one substrate" are provided for (Example 2 and 4 teach only a PHB polymerase gene from *A. caviae* and the *phbAB* genes from *R. eutropha*), given the production of PHB-co-HH cited in the Examples is at the level of only 1% of the total product it is clear that the reaction that produces PHB-co-HH is not efficient or favored by the enzymes taught in the examples and given the broad genus of enzymes that comprise the invention the Examiner maintains that one of skill in the art would be required to practice undue trial and error experimentation testing the non-exemplified enzymes in combination for converting substrate to PHB-co-HH polymer.

Applicant asserts that the consideration given by the Examiner to secondary pathways is undue and unnecessary in view of the production of PHB-co-HH using a broad range reductase and a polymerase that accepts 3-HH-CoA and 3-HB-CoA as substrate (response page 8). Applicant's arguments are unpersuasive in view of the lack of examples of combinations of enzymes from a multitude of sources that would produce PHB-co-HH polymer.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Russell Kallis Ph.D.  
May 31, 2003



***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

8. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Russell Kallis Ph.D.  
May 31, 2003

A handwritten signature in black ink, appearing to read "Amy Nelson", written in a cursive style.

AMY J. NELSON, PH.D  
SUPERVISORY PATENT EXAMINER  
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